Effect of povidone-iodine on wound healing: A review

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For the purpose of providing a summary of current clinical trials to determine whether povidone-iodine is beneficial or detrimental to wound healing, an integrated review was completed. Clinical trials were defined as any study that uses some concentration and form of povidone-iodine in a comparison or evaluation with other products or treatments resulting in an impact of povidone-iodine on wounds. The use of povidone-iodine for cleansing, irrigating, and dressing wounds is controversial. Wound healing is complex and requires safe and effective treatment modalities. Numerous in vitro and in vivo studies have been done with conflicting results on bactericidal effects and cytotoxicity of this antimicrobial agent. Human and animal in vivo studies in the last 10 years were used for this review because often the relevance of in vitro data in clinical conditions are questioned. The varied studies provide evidence that in most instances, povidone-iodine did not effectively promote good wound healing; in fact, most studies showed either impaired wound healing, reduced wound strength, or infection. (J Vasc Nurs 1999;17:17-23.)

Povidone-iodine is a commonly used antimicrobial agent that contains polyvinylpyrrolidone iodine, which is a water-soluble complex with elemental iodine bound to a synthetic polymer. The bactericidal component is free iodine (usually 1 ppm), which is liberated gradually from the polyvinylpyrrolidone iodine.[1] The most commonly manufactured form is a 10% solution in water. It is a bactericide/virucide for application as a paint, spray, or wet soak for the treatment of lacerations, abrasions, second-degree and third-degree burns, and as a prophylactic anti-infective agent for incisions, thrush, skin infections, decubitus and stasis ulcers, and preoperatively in swabbing the mouth and throat. In addition to this solution, povidone-iodine is available in a 7.5% concentration scrub with detergent for preoperative and postoperative scrubbing in the operating room and as a germicidal wash. The water-soluble ointment provides a 10% concentration of polyvinylpyrrolidone iodine in a polyethylene glycol base for use in infected surgical incisions, infected pressure or stasis ulcers, pyrodermas, and traumatic lesions. A first aid cream is available that provides a 5% concentration of polyvinylpyrrolidone iodine in an oil-in-water emulsion for use in open cuts, burns, or scrapes.[2] In addition, a dry powder spray that contains 2.5% povidone-iodine and Savlodil (Wyeth-Ayerst, Division of American Home Products Co, Philadelphia, Pa) sterile solution (chlorhexidine gluconate 0.015%/cetrimide 0.15% in 100 mL sachets) recently has been developed.[3]

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The use of povidone-iodine is one of the most controversial issues in wound care. Current literature regarding the cytotoxicity of povidone-iodine is conflicting. Even though some studies show impairment of wound healing, other studies reflect improved wound healing with the use of povidone-iodine.[3-12] It continues to be available in health care facilities, and many physicians order it for cleansing, irrigating, or dressing wounds.

Wound healing is complex and accomplished by a series of events involving 3 phases (ie, the inflammatory phase, the proliferative phase, and the maturation phase) (Table I). The healing process applies to all wounds regardless of the nature, type, or size. A simple skin tear uses the same steps in healing that are found in burn wounds, pressure sores, surgical incisions, or vascular ulcers. Optimal wound management requires the selection of the most appropriate treatment, which is a treatment that will influence this dynamic series of events swiftly and efficiently. Methods of wound care have changed for the better. The focus for wound care is primary prevention: eliminating causative factors (pressure, shear, friction, moisture, circulatory impairment, and neuropathy) and providing systemic support (good nutrition and fluids and systemic antibiotics) instead of scrubbing wounds and leaving them open to the air.[15] Nurses are now using proper cleansing techniques (a physiologically compatible cleansing agent such as normal saline and elimination of trauma) and applying appropriate topical therapy (remove necrotic tissue, identify and eliminate infection, obliterate dead space, absorb excess exudate, and maintain moist wound environment), and protecting the healing wound with an appropriate cover dressing.[16]

A wound, whether acute or chronic, is an insult to the body's integrity. Minimal chemical (application of an agent that is not physiologically compatible) and mechanical (pressure, shear, friction, or scrubbing of the wound) trauma should be applied when cleansing wounds.[16] In wound treatment, additional trauma to the wound base delays wound repair.[17] Disturbance of the wound should be kept to a minimum not only to avoid further tissue damage but also to eliminate unnecessary discomfort for the patient and to decrease the possibility of the spread of microorganisms.[18]

A panel of multidisciplinary experts in the field of skin and wound care were appointed in 1989 by the US Department of Health and Human Services to develop guidelines for prevention, assessment, and treatment of pressure ulcers. These guide-

TABLE I.

WOUND HEALING[1,13,14]

Phases	*Occurrence*	*Events*	*Key cell*
Inflammatory	The body's immediate response to injury	Vasoconstriction: Constricted vessel allows clotting of blood to seal wound Vasodilation:Swollen vessel brings more blood and plasma components to wound site	Polymorphonuclear leukocytes: white cells Clean wound site Provide resistance to micro-organisms Scavengers of tissue debris/ foreign materials
		Increased permeability: Allows more white cells to travel through the vessel wall to combat foreign bodies	Monocytes: Intermediary white cells Replace polymorphonuclear leukocytes with similar function Become macrophages
		Cellular response: White cells ingest bacteria, debris and dead cells, then build up in plasma, forming pus	Macrophages: Most common white cells Major mediator of inflammation and repair in wound healing
Proliferative	Tissue regeneration for body repairs	Granulation: Cells migrate into the wound and fill in (usually red tissue) Epithelialization: Epidermis slides across and forms over surface. Contracture: Scar is formed and wound can withstand normal stresses	Fibroblasts: Cells that establish, maintain, and repair tissues Release collagen into the wound bed to produce new granulation tissue and pull on collagen fibers for wound contracture
Maturation	Remodeling	Strengthening of the scar occurs by the consolidation of collagen fibers Regains near 80% original tissue strength	Macrophages Fibroblasts

lines promote the use of normal saline for cleansing most pressure ulcers and discourage the use of skin cleansers or antiseptic agents (eg, povidone-iodine, iodophor, sodium hypochlorite solutions [Dakin's solution], hydrogen peroxide, and acetic acid) because they are reactive chemicals that are cytotoxic to normal tissues.[16] Topical agents should allow the body's own defense mechanisms to function for inhibition of antimicrobial growth in a wound when the immune response is effective. If the body's response to injury is inadequate as in the case of a severe burn, more aggressive treatment must be considered. According to Rodeheaver,[17] topical antibiotics are the only antimicrobial agents that should be used in wounds.

PURPOSE OF REVIEW

The purpose of this review was to determine safety and effectiveness of povidone-iodine in the treatment of acute and chronic wounds by using current research. There are researchers whose names appear frequently in studies involving povidone-iodine, but most cited studies in current literature were done 15 to 20 years ago. The extensive work of Lineaweaver et al[19,20] is frequently referenced, showing cytotoxic effects of povidone-iodine and other topical antimicrobial agents on human fibroblasts and keratinocytes. This research found that 1% povidone-iodine solutions were toxic to fibroblasts but a 1:1000 dilution of the 1% solution (0.001%) caused no fibroblast toxicity and remained bactericidal to *Staphylococcus aureus*. Fibroblasts are the key cells for laying down the collagenous scar tissue and are involved with contraction (Table I).

Rodeheaver et al[21] published findings on bactericidal effects and cytotoxicity of iodine-containing solutions. Rodeheaver used a study by Robsin to show that bacteria are reduced more effectively by using normal saline wet-to-dry dressings than with povidone-iodine. Studies also were cited that verified lower infection rates by using normal saline compared with povidone-iodine wound irrigations. Rodeheaver's well-known studies demonstrate the deterioration of fibroblasts, monocytes, and granulocytes when treated with povidone-iodine. Fibroblasts, keratinocytes, and leukocytes are necessary for wounds to heal (Table I). In 1919 Alexander Fleming[22] found that:

> "Antiseptic solutions show their maximum bactericidal action when they are allowed to act on the microbes in a watery medium; their action is more feeble when the medium is of a serous character; it is still less in blood; it is further reduced when the medium is of a purulent nature;

while least of all will an antiseptic act on bacteria embedded in a piece of tissue."

Iodine was one of the antiseptics tested. These studies are important, but because of continuing questions about the use of povidone-iodine in wounds, the findings of more recent studies are of interest.

In addition, much of the research on povidone-iodine involves in vitro studies. Teepe et al[23] used in vitro toxicity testing with epidermal cell culture systems and found it to be fast, reproducible, and objective, which gives it a major advantage over subjectively assessed animal tests. Even though Teepe et al presents this view, often the relevance of use of in vitro data in clinical conditions is questioned.[24,25] For that reason, in vivo studies were chosen for this review.

SCOPE

As a result of the controversy involving the use of povidone-iodine in wound care, I reviewed all studies published in the last 10 years. Clinical trials were defined as any study that used some concentration and form of povidone-iodine in a comparison or evaluation with other products or treatments, which resulted in the impact of povidone-iodine on wounds. All studies did not achieve statistical significance.[3,4] Some studies did not acknowledge statistical significance in their findings.[5,6] One study was a quality research study in which data were obtained from charts of patients who had received wound treatments that used standard protocol with povidone-iodine.[7] This information was compared with a new protocol eliminating povidone-iodine. Studies were located by using the key words "povidone-iodine" and "wound care," and were obtained from CINAHL and Medline (Tables II and III).

INCLUSION

All in vivo animal and human clinical trials published from 1988 to 1998 that were found, regardless of the animal type, placement and type of wounds being treated, purpose of the actual study, and the concentration or form of povidone-iodine, were used in the review.

EXCLUSION

Exclusion criteria included studies of wounds treated with povidone-iodine only (no comparison or control group), in vitro studies, non-English publications, and studies published before 1988.

TRIAL METHODS

Animal Subjects

A total of 272 animal subjects participated in the trials, which ranged from 3 to 99 subjects per trial (Mean [M] = 54.4, SD = 34.3). Subjects consisted of pigs, mice, rats, and guinea pigs. In most cases, wounds were produced through surgical incision; some wounds were clean and other wounds were impregnated with various bacteria. Subjects had multiple wounds of the same size and type to produce accurate comparisons.

Human Subjects

A total of 436 human subjects participated in the trials, which ranged from 11 to 248 subjects per trial (M = 87.2, SD = 95.3). One of the human studies compared 2 actual chronic wounds of similar size and type on each person, which gave a true comparison with the person serving as his own control.[4] Only one study used clinically produced wounds.[8] The other studies were actual cases at health care facilities for some type of wound care.

Analysis

The number of comparisons and measurements varied (maximum = 7). The effects of povidone-iodine were recorded in respect to the other treatment modalities. If one result was found to be significant, the study was counted as reaching significance. The studies were different in purpose, which may account for discrepancies between studies, including such factors as (1) methods used for assessing epithelialization, (2) product bias, (3) control groups, (4) skin types and healing rates, (5) strengths and preparations of povidone-iodine, and (6) types of dressings.

OVERVIEW OF STUDIES

Animal Studies

A variety of animals is included in this review. Some of the researchers provided reasons for the type of animal used in their studies, and most researchers provided relevant information about the area (location and tissue type) of the animal used for wounding and clearly delineated methods and products used in treating the wounds (Table II). All of the animal studies resulted in impaired or delayed wound healing with the use of povidone-iodine, and only 1 of the 5 studies did not acknowledge statistical significance.[5]

The majority of animal studies involved rodents: mice, guinea pigs, or rats. Two of the animal studies were done with mice.[9,10] Mice are loose-skinned mammals. Their skin contains subcutaneous panniculus carnosus muscle, which is not found in tight-skinned humans.[9] According to the authors, the panniculus may significantly contribute to wound healing, and the nutritional requirements for healing in mice differ from that of humans. Molloy and Brady[11] used the panniculus carnosus muscle of rats for their study. The ears of mice, which have a central cartilaginous sheet between 2 thin layers of skin consisting of epidermis and vascular connective tissue, were the subjects of study by Kjolseth et al.[10]

Studies by Hartwell and Winter (as cited in Archer et al[5]) found pigs to be the most suitable animal for studying full thickness wound healing because their epidermis, dermis, and subcutaneous fat closely resemble that of the human. Archer et al[5] chose pigs because of this similarity. Although the sample is small, this study could be the most valuable animal study reviewed because of the close similarities of pig tissues to human tissues. Povidone-iodine caused a delay in wound healing in 2 of 4 wounds, and when compared with film dressings and sugar paste, showed no reduction in bacterial growth. This study was the only study that addressed the antiseptic effect of povidone-iodine and other antiseptics on wounds. It was found that bacterial colonization did not impair formation of collagen

TABLE II.

SUMMARY OF RESEARCH DESIGNS AND OUTCOMES INVOLVING POVIDONE-IODINE—ANIMAL STUDIES

Reference	*Sample*	*Study design*	*Study purpose*	*Results of povidone-iodine use*
Archer et al[5]	Pigs (N = 3) 4 sites/pig Surgically incised full-thickness wounds (up to 9 mm deep)	Controlled laboratory, single blind	Comparison between semipermeable film, antiseptics, and sugar paste in wound care	With 0.8% povidone-iodine impregnated gauze every 48 hours, at 7 days, impaired healing with large numbers of bacteria Statistical significance not stated
Kashyap et al[9]	Female mice (N = 60) Surgically incised and sutured wounds	Random, controlled laboratory, blind	To evaluate the effect of topical povidone-iodine ointment on wound healing	Povidone-iodine applied daily for 7 days, significantly reduced wound strength Statistically significant†
Kjolseth et al[10]	Adult male hairless Mice (N = 99) sugical ly incised circular full-thickness wounds (0.125 mm deep)	Controlled laboratory	Comparison effects of commonly used wound agents on wound healing	10% povidone-iodine, applied daily covered with gauze until healed, delayed epithelialization, enhanced early neovascularization Statistically significant*†
Menton and Brown[12]	Adult guinea pigs (N = 60) Surgically incised full-thickness wounds	Controlled laboratory, double blind	Comparison effects of 2 wound cleansers to Betadine surgical scrub and NS at intervals of 3, 6, 9, 14, and 21 days	Betadine surgical scrub applied daily caused irritation,* retarded epidermal and dermal healing,* prolonged inflammation,* and increased tensile strength*
Malloy and Brady[11]	Male rats (N = 50) Surgical paravertebral incisions dividing deep panniculus carnosus muscle with loose primary closure	Controlled laboratory	The effect of a wick (with either povidone-iodine or NS) on healing in clean uncontaminated wounds	1% Povidone-iodine, daily soaked ribbon gauze × 3 days: Prolonged impairment of healing in wicked wounds and adjacent unwicked wounds (with no povidone-iodine) Statistically significant*†

*$P < .01$.
†$P < .05$.
NS, Normal saline.

tissue or epidermal migration. No wound infections occurred. Gauze dressings were applied to the wounds treated with antiseptics. Cotton fibers from the gauze were found in the new connective tissue, which could have been responsible for disruption of the natural healing process. According to the authors, it appeared that "the antibacterial action of povidone-iodine was neutralized by protein binding at the concentration used but there was sufficient activity remaining to delay wound healing." The data presented in their study support harmful and possibly counterproductive treatment with povidone-iodine.

Three of the studies found conflicting results on wound strength from the use of povidone-iodine. Kashyap et al[9] found a reduction in wound strength compared with the control group by using topical povidone-iodine ointment. Although not specified, the manufactured concentration of povidone-iodine in ointment is 10%. The authors concluded that povidone-iodine ointment "may be deleterious to wound healing and potentially harmful" in its application to clean lacerated wounds. Tensile wound strength increased in the study by Menton and Brown[12] that used Betadine Surgical Scrub (The Purdue Frederick Company, Norwalk,

TABLE III.

SUMMARY OF RESEARCH DESIGNS AND OUTCOMES INVOLVING POVIDONE-IODINE—HUMAN STUDIES

Reference	*Sample*	*Study design*	*Study purpose*	*Results of povidone-iodine use*
Connell[7]	Human emergency department patients (N = 92), acute wounds requiring suturing	Quality assurance study, no controlled design, 1 chart reviewer	Audits comparing wound preparation by doctor preference (including Betadine, pHisoHex (Sanofi Winthrop Pharmaceuticals, New York, NY) hydrogenperoxide, or NS) and preparation with a standardized protocol of NS or Shur-Clens (Calgon Vestal Laboratories, St Louis, Mo) and NS	With the elimination of povidone-iodine and implementation of new wound cleansing protocols, infection rates were decreased from 11.9% to 6%
DeKock et al[6]	Human burn patients (N = 60), acute superficial and deep burn wounds at burn unit	Controlled laboratory, random assignment	Comparison of povidoneiodine to silver sulphadiazine in the topical treatment of flame and fluid burn wounds	With 5% povidone-iodine cream, mild to moderate discomfort on application but more successful in treatment and less bacteria cultured from wounds than with 1% silver sulphadiazine Statistical significance not addressed
Gordon[3]	Human emergency department patients (N = 248), upper limb cuts all contaminated to some extent, requiring sutures	Controlled laboratory, random, blind, single assessor	Comparison of efficacy of Betadine Dry Powder Spray (2.5% povidone-iodine) and Savlodil sterile solution (0.075% chlorhexidine and 0.015% cetrimide)	After 5 to 8 days (physician's decision) 18% infection rate with povidone-iodine No serious infections No significant difference
Hopf et al[8]	Human subjects (N = 25), unroofed clinically blisters equivalent to superficial abrasions or second-degree burns	Controlled laboratory, random assignment	Comparison of Betadine Cream, Silvadene Cream, (American Home Products Company, Philadelphia, Pa) and no treatment to determine influence on rate of healing in uninfected wounds	With 5% Betadine Cream, 100% epithelialization faster than Silvadene Cream and no treatment, and less crusting on wounds compared with no treatment Statistically significant*
Saydak[4]	Human men (N = 11), mean age = 64, each with at least 2 pressure ulcers of compatible length and depth (served as own controls)	Research project, controlled laboratory, 1 investigator	Comparison of absorption dressing with treatment protocol of povidone-iodine, NS rinse, and dry sterile dressing 3 times daily	1% povidone-iodine treatment produced slower healing No significant difference

*P < .01.
NS, Normal saline.

Conn), which contains 7.5% polyvinylpyrrolidone-iodine and 0.75% free iodine plus anionic detergent, in wounds of guinea pigs. Histologic examinations did not reveal greater collagen production, but the authors indicate the fibroarchitecture of the collagen may have caused the stronger and less elastic dermis. The indication for use of this product is as a skin cleanser.[2] According to Goldenheim,[26] who is affiliated with The Purdue Frederick Company, it is the detergent base of the scrub, which contains ammonium nonoxynol-4-sulphate and lauramide DEA, not the povidone-iodine, responsible for detrimental effects to the tis-

sues. The deleterious effects of the scrub and the increased tensile strength found in this study may or may not be caused totally to the detergent. More study is needed.

Molloy and Brady[11] found that the use of a saline wick delayed healing as long as 15 days and the use of a 1% povidone-iodine wick delayed healing as long as 30 days. Even though much care was taken to avoid cross-over contact by the 2 adjacent wicked wounds, in addition to a reduction in wound-breaking strength of the povidone-iodine wicked wounds, the control wounds located 2 cm away from the povidone-iodine wicked wounds also showed a reduction in wound-breaking strength. The authors speculate that both local diffusion and systemic absorption of iodine accounted for delayed healing in the control group. Two cases potentiate their speculation. Shetty and Duthie[27] published a case study of an elderly man with no goiter and a normal radioiodine uptake in his thyroid gland who had iodide-induced thyrotoxicosis caused by increased serum iodine availability through povidone-iodine soaks to his multiple pressure sores. D'Auria et al[28] reported a case of systemic iodine toxicity when povidone-iodine solution was used as a continuous postoperative wound irrigation after hip wound debridement. The patient died in 10 hours with a serum total iodine concentration 1000 times the normal level. System iodine absorption appeared to cause her death. Burks[29] reviewed other reports of systemic toxicity from similar treatments that involve povidone-iodine.

Kjolseth et al[10] found that neovascularization occurred significantly earlier with povidone-iodine than with silver nitrate, but overall, only slight differences were found in the time it took different agents (control, silver sulfadiazine, mafenide acetate, silver nitrate, bacitracin, and povidone-iodine) to reach complete neovascularization. Even with faster neovascularization, epithelialization with povidone-iodine was significantly slower than with any of the other tested agents.

Human Studies

Outcomes from studies of human subjects were not as conclusive as outcomes from studies of animal subjects. The reason appears to be the varied purposes of the studies done and the absence of good controls (Table III).

Connell[7] showed a decreased infection rate (from 11.9% to 6%) when povidone-iodine was eliminated from the wound cleansing protocol. An 18% infection rate was found by Gordon et al[3] when povidone-iodine was used. The implication is that topical povidone-iodine does not eliminate wound infections. DeKock et al[6] found that povidone-iodine produced mild to moderate discomfort on application but more successful treatment results and less bacteria in burn wounds than those treated with silver sulfadiazine. *Staphylococcus aureus* was cultured in both groups. It is interesting that 80% of the bacteria found in wounds treated with povidone-iodine was *Staphylococcus aureus* compared with 52% of the bacteria in wounds treated with silver sulfadiazine. The bacteria from the silver sulfadiazine-treated wounds also contained 36% β-haemolytic *Streptococcus,* but none was found in the cultures from the povidone-iodine treated wounds. Nineteen wounds treated with silver sulfadiazine were cultured compared with only 10 wounds treated with povidone-iodine. Reasons for this difference were not noted. A confounding variable of this study was that 7 subjects being treated with silver sulfadiazine, after showing systemic signs of infection, were changed to treatment with povidone-iodine, which was successful.

Hopf et al[8] reported fewer days to reach 100% re-epithelialization with povidone-iodine compared with silver sulfadiazine and the "no treatment" control. However, on day 7 of the study, povidone-iodine had more epithelium coverage and less crusting than the "no treatment" control group on clinically produced blisters (similar to superficial abrasions or second-degree burn wounds). The authors did not comment on the epithelial growth or crusting of the silver sulfadiazine group on the seventh day. According to the authors, "Betadine Cream was statistically superior to Silvadene Cream with regard to healing of experimental wounds." This study was done in affiliation with The Purdue Frederick Company, Norwalk, Connecticut, which is a major producer of povidone-iodine.

The evidence from these 2 studies[6,8] found that the use of povidone-iodine was superior to silver sulfadiazine in the treatment of burn wounds. Because the wounds produced in the Hopf[8] study were equivalent to superficial abrasions or second degree burns, it would be interesting to trial the use of normal saline for cleansing and either a film or hydrogel to provide a moist wound healing environment as an additional treatment modality with povidone-iodine and silver sulfadiazine. Severe burn wounds are different from other skin wounds and require different treatment. Perhaps studies of burn wounds should be reviewed separately from other wounds. In a review of the use of povidone-iodine in burn treatments, Steen[30] discussed in depth the severe problems of local infection and burn wound sepsis. Because of broad bacterial action and its ability to penetrate eschar, Steen[30] concluded that povidone-iodine is well suited for burn surface therapy. However, he cautions its use for granulating or recent surgically excised tissue.

Although the research project by Saydak[4] was not a formal study, the use of human subjects serving as their own controls provides information that cannot be ignored. Because both treatment modalities were used in the same subject, factors of age, medications, motility, nutrition, and presence of disease were the same for each. The ulcers treated with povidone-iodine did not show reduced ulcer depth as did those with the absorbent dressing and continued to lag behind in depth reduction throughout the study. Statistical significance between treatment types was not found, which may be a result of the application of a dry control dressing or the small sample size. In addition, the author did not state that cleansing methods were used in the control wounds. Pressure ulcers require dressings that will maintain their physiologic integrity and provide a moist healing environment. Careful wound cleansing removes dressing residue, wound exudate, and metabolic wastes. It would be of interest to see a study of this type with normal saline cleansing and a hydrogel dressing or use of a sugar paste as in the study by Archer et al[5] as comparisons.

CONCLUSIONS

A review of the literature has shown reasonable evidence to question the benefits of povidone-iodine in wound healing. Even though the number of subjects is small, the purpose of the stud-

ies was very different, which provides evidence that in most instances, povidone-iodine did not effectively promote good wound healing. In fact, 8 of the 10 studies showed either impaired wound healing, reduced wound strength, or infection in open wounds treated with povidone-iodine. The 2 remaining studies showed povidone-iodine to be more successful than silver sulfadiazine in the treatment of burn wounds, which are so different from other wounds that specific methods of treatment should be researched separately.

When selecting treatment, the type and characteristics of the wound and the subject's immune response must be considered. From the evidence presented in this review, povidone-iodine may be deleterious to the wound. Proper cleansing with a physiologically compatible agent such as normal saline, elimination of mechanical trauma and pressure, and providing a moist wound environment should be the treatment of choice for good wound care after treatment of the underlying condition and removal of necrotic tissue has been accomplished. Guidelines from experts in skin and wound care promote this type of treatment and discourage the use of povidone-iodine as a result of its cytotoxic effects to normal tissues. In addition, iodine toxicity from the use of povidone-iodine in open wounds must be considered. Further studies of the interactions of povidone-iodine, bacteria, and the immune system are needed to determine whether clinical situations exist in which the use of povidone-iodine is beneficial.

REFERENCES

1. Doughty D. A rational approach to the use of topical antiseptics. J Wound Ostomy Continence Nurs 1994;21:224-31.
2. The Purdue Frederick Company. Betadine microbicides. Package insert. 1998. Norwalk, Conn.
3. Gordon MWG, Aikman L, Little K, Luke C. Prevention of wound infection in the accident and emergency department: does povidone iodine dry powder spray reduce infection rates? Br J Accident Emerg Med 1989;4:11-3.
4. Saydak SJ. A pilot test of two methods for the treatment of pressure ulcers. J Enterostomal Ther 1990;17:139-42.
5. Archer HG, Barnett S, Irving S, Middleton KR, Seal DV. A controlled model of moist wound healing: comparison between semi-permeable film, antiseptics and sugar paste. J Exp Pathol 1990;71:155-70.
6. DeKock M, Van der Merwe AE, Swarts C. A comparative study of povidone iodine cream and silver sulfadiazine in the topical treatment of burns. Wounds 1989;1:65-71.
7. Connell S. A two-part quality assurance project addressing infection rates of wounds sutured in the emergency department. J Emerg Nurs 1991;17:212-4.
8. Hopf K, Grady R, Stahl-Bayliss C, Fitzmartin R. The effect of betadine cream vs silvadene cream on reepithelialization in uninfected experimental wounds. Proceedings Am Burn Assoc 1991;23:166.
9. Kashyap A, Beezhold D, Wiseman J, Beck WC. Effect of povidone iodine dermatologic ointment on wound healing. Am Surg 1995;61:486-91.
10. Kjolseth D, Frank JA, Barker JH, Anderson GL, Rosenthal AI, Acland RD, et al. Comparison of the effects of commonly used wound agents on epithelialization and neovascularization. J Am Coll Surg 1994;179:305-12.
11. Molloy RG, Brady MP. A modified technique of delayed primary closure using a povidone iodine wick: influence on wound healing in an experimental model. Irish J Med Sci 1993;162:297-300.
12. Menton DN, Brown M. The effects of commercial wound cleansers on cutaneous wound healing in guinea pigs. Wounds 1994;6:21-7.
13. Perry AG, Potter PA, Clinical nursing skills and techniques. St Louis (MO): Mosby; 1998. p. 1134.
14. Taylor C, Lillis C, LeMone P. Fundamentals of nursing: the art and science of nursing care. Philadelphia (PA): JB Lippincott Co, 1266.
15. Bryant RA, editor. Acute and chronic wounds: nursing management. St Louis (MO): Mosby; 1992.
16. Bergstrom N, Bennett MA, Carlson CE, et al. Treatment of pressure ulcers. Clinical practice guideline, No. 15. AHCPR Publication No. 95-0652. Rockville (MD): US Department of Health and Human Services. Public Health Service, Agency for Health Care Policy and Research; Dec 1994.
17. Rodeheaver G. Controversies in topical wound management. Wounds 1989;1:19-27.
18. Raggett L. Management of infected wounds. Nurs Standard 1992;6(25):29-30.
19. Lineaweaver W, Howard R, Soucy D, McMorris S, Freeman J, Crain C, et al. Topical antimicrobial toxicity. Arch Surg 1985;120:267-70.
20. Lineaweaver W, McMorris S, Soucy D, Howard R. Cellular and bacterial toxicities of topical antimicrobials. Plastic Reconstructive Surg 1985;75:394.
21. Rodeheaver G, Bellamy W, Kody M, Spatafora G, Fitton L, Leyden K, et al. Bactericidal activity and toxicity of iodine-containing solutions in wounds. Arch Surg 1982;117:181-5.
22. Fleming A. The action of chemical and physiological antiseptics in a septic wound. Br J Surg 1919;7:99-129.
23. Teepe RGC, Koebrugge EJ, Lowik CWGM, Petit PLC, Bosboom RW, Twiss IM, et al. Cytotoxic effects of topical antimicrobial and antiseptic agents on human keratinocytes in vitro. J Trauma 1993;35:8-19.
24. Niedner R. Cytotoxicity and sensitization of povidone-iodine and other frequently used anti-infective agents. Dermatology 1997;195(Suppl 2):89-92.
25. Gilchrist B. Should iodine be reconsidered in wound management? J Wound Care 1997;6:148-50.
26. Goldenheim PD. An appraisal of povidone-iodine and wound healing. Postgrad Med J 1993;69(Suppl 3):S97-S105.
27. Shetty KR, Duthie EH. Thyrotoxicosis induced by topical iodine application. Arch Intern Med 1990;150:2400-1.
28. D'Auria J, Lipson S, Garfield JM. Fatal iodine toxicity following surgical debridement of a hip wound: case report. J Trauma 1990;30:353-5.
29. Burks RI. Povidone-iodine solution in wound treatment. Phys Ther 1998;78:212-8.
30. Steen M. Review of the use of povidone-iodine (PVP-I) in the treatment of burns. Postgrad Med J 1993;69(Suppl 3):S84-S92.